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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/747,004	12/21/2000	Jing-Shan Hu	3366.1	2941

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EXAMINER
SIEW, JEFFREY

ART UNIT	PAPER NUMBER
1637	17

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/747,004	Applicant(s) HU ET AL.	
	Examiner Jeffrey Siew	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Request for Continued Examination

The request filed on 1/13/03 for a Request for Continued Examination (RCE) under 37 CFR 114 is acceptable. An action on the RCE follows. Pending claims are 1-24.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-16,18 & 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urdea et al (US4,868,105 Sept. 19, 1989) in view of Lockhart et al (6,040,138 March 21, 2000).

Urdea et al teach the detection of target nucleic acid using two sets of probes on a support. (see whole doc. esp. abstract). One is bound to support and contains a region that binds

to a recognition region of the second probe. The second probe contains a region that binds to target nucleic acid (see col. 1lines 41-61 and Figure 1A). They teach the subset regions will have at least 15 or at least 25 nucleotides. (see col. 2 line 56-60). They teach that labels may be fluorescers (see col.3 line 39 and detected by pandex screen machine (see 13 line 54). They teach that analyte samples may be any nucleic acids from biological fluids (see col.4 line 1-2).

Urdea et al do not explicitly teach 50 different cipher probes.

Lockhart et al teach expression monitoring on high density array with bound olignucleotide arrays in which more than 100 different oligonucleotides may be bound (see whole doc. esp. abstract). They teach a density of greater than 1000 oligonucleotides per cm2 (see col .3 line 15). They teach light directed polymer synthesis for constructing immobilized oligonucleotides (see col. 3 line 47). They also teach detection with fluorescence microscope to detect patterns (see col. 2 line 28 & col. 3 line 67). They teach detecting form mRNA or cDNA from biological samples(see col.4 lines 8-12).

One of ordinary skill would have been motivated to combine Lockhart et al's multiple probes and lengths to Urdea et al's assay to in order to detect a multiplicity of genes. Lockhart et al teaches that multiple bound oligonucleotides provide greater simultaneous analysis of different targets. It would have been prima facie obvious to apply Lockhart et al's teaching of multiple probes to Urdea et al's support in order to provide a high throughput analysis of multiple genes with high signal to noise ratio.

2. Claims 17 & 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urdea et al (US4,868,105 Sept. 19, 1989) in view of Lockhart et al (6,040,138 March 21, 2000) in further view of Vinayak et al (US6,225,476 July 3, 2001).

The teachings of Lockhart et al and Urdea et al are described previously.

Urdea et al do not teach 5-3 or 3-5 synthesis.

Vinayak et al teach 5-3 or 3-5 synthesis (see col.5 line 62-62 & col. 10 line 11 -20).

One of ordinary skill in the art would have motivated to apply synthesis in order to construct oligonucleotides in the direction that would bind to Urdea second probes. It was well known and commonly practiced in the art to synthesize the oligonucleotides in either direction, it would have been prima facie obvious to apply the synthesis of Vinayak et al in order to create oligonucleotides that would optimally hybridize in the direction of the complementary target.

3. The response filed 12/16/02 to the prior art rejections has been fully considered and deemed not persuasive. The response states that Urdea do not teach or provide suggestions for at least 50 different cipher probes in microarray assays. They further contend that adding large number of mediator probes would increase complexity of microarray based assays.

First of all, the claims do not recite a limitation of microarray format per se but recite a broad generic term "substrate". Such language would encompass any support that was well known and commonly practiced in the art at the time the invention was made including filters, microtiter plates, glass supports etc. as taught by Urdea (see Urdea col.4 lines 55-60). While not necessarily conceding to the response's position that Urdea's teaching would not also be applicable to microarray format, this argument proves not particularly relevant in light of the

claim interpretation. The claims do not explicitly recite the microarray format. The 103 rejection bases its premise that Lockhart's **teachings of constructing and using support bound 100 different probes** to detect different targets would be **applied toward** Urdea et al's support. e.g. microtiter plates, filters etc, The limitation of at least 50 different probes e.g. the probes may be met by the probes occupying different wells of the microtiter plate. It would have been in the within the skill of one of ordinary skill in the art at the time the invention was made to detect at least 50 different support bound probes to target different nucleic acids using the combination of Lockhart et al and Urdea et al. Moreover, reading a hybridization pattern is not limited to solely microarray formats but is used in almost every hybridization assay in determining which position or spots hybridization occurred e.g. on southern filters, microtiter wells etc. The previously made prior art rejections are maintained.

THE FOLLOWING IS A NEW GROUND OF REJECTION NECESSITATED BY THE AMENDMENT AND NEW SEARCH

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The term "the mediator nucleic acids" lacks antecedent basis. It cannot be determined as to what mediator nucleic acids are being referred to and therefore the limitations of those nucleic acids cannot be determined.

4. Claims 1-16,18 & 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (6,150,095 Nov. 21, 2000) in view of Lockhart et al (6,040,138 March 21, 2000).

Southern et al teach a method of detecting targets. They teach an ASO probe is bound to support which would meet an cipher probe.(see whole doc. esp. figure 3). They teach an intermediate polynucleotide which binds to the bound ASO probe and also another target that ultimately leads to ligation.

Southern et al do not explicitly teach 50 different cipher probes.

Lockhart et al teach expression monitoring on high density array with bound olignucleotide arrays in which more than 100 different oligonucleotides may be bound (see whole doc. esp. abstract). They teach a density of greater than 1000 oligonucleotides per cm2 (see col .3 line 15). They teach light directed polymer synthesis for constructing immobilized oligonucleotides (see col. 3 line 47). They also teach detection with fluorescence microscope to detect patterns (see col. 2 line 28 & col. 3 line 67). They teach detecting form mRNA or cDNA from biological samples(see col.4 lines 8-12).

One of ordinary skill in the art would have been motivated to apply Lockhart et al's teachings of 100 different oligonucleotides to Southern et al's method of analyzing sequences in order to detect multiple samples. Lockhart et al teaches that multiple bound oligonucleotides provide greater simultaneous analysis of different targets. It would have been prima facie

obvious to apply Lockhart et al's array to Urdea et al's probes in order to provide a high throughput analysis of multiple genes with high signal to noise ratio.

Southern et al's prior art rejection was raised to meet the microarray embodiment within the scope of the claims. Moreover, while Southern et al has named their probes as "cipher" or "mediator nucleic acids", they do teach ASO probes and hybridized polynucleotides in the ligation reaction that would meet the functional limitations of the cipher and mediator probes as described in the claims and the specification see page 19 & 20.

5. Claims 17 & 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (6,150,095 Nov. 21, 2000) in view of Lockhart et al (6,040,138 March 21, 2000) in further view of Vinayak et al (US6,225,476 July 3, 2001).

The teachings of Southern et al and Urdea et al are described previously.

Southern et al do not teach 5-3 or 3-5 synthesis.

Vinayak et al teach 5-3 or 3-5 synthesis (see col.5 line 62-62 & col. 10 line 11 -20).

One of ordinary skill in the art would have motivated to apply synthesis in order to construct oligonucleotides in the direction that would bind to Urdea second probes. It was well known and commonly practiced in the art to synthesize the oligonucleotides in either direction, it would have been prima facie obvious to apply the synthesis of Vinayak et al in order to create oligonucleotides that would optimally hybridize in the direction of the complementary target.

SUMMARY

6. No claims allowed.

CONCLUSION

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail address is Jeffrey.Siew@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner is on flex-time schedule and can best be reached on weekdays from 6:30 a.m. to 3 p.m. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119.

Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Tracey Johnson for Art Unit 1637 whose telephone number is (703)-305-2982.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-3290 and Before Final FAX (703) 872-9306 or After Final FAX (703) 30872-9307.

JEFFREY SIEW
PRIMARY EXAMINER
3/23/05